REMARKS

1. Preliminary Remarks

a. Status of the Claims

Claims 26, 31, 33, and 35-37 are pending and under active consideration in this application. Claims 1-25, 27-30, 32, 34, and 38-40 have been previously canceled. Applicant respectfully requests entry of the remarks made herein into the file history of this application.

2. Patentability Remarks

a. 35 U.S.C. § 102

At pages 2-4 of the Office Action, the Examiner reinstates the rejection of claims 31 and 36 under 35 U.S.C. § 102(b) as allegedly being unpatentable over Ghazal (WO200257437; "Ghazal"). Applicant respectfully disagrees. Applicant respectfully submits that the Examiner has failed to consider each and every element of the claims.

Claims 31 and 36 currently read as follows (emphasis added):

> 31. A vector **comprising** a **heterologous** sequence, wherein the **heterologous** sequence is selected from the group **consisting** of
>
> (a) SEQ ID NO: 4204050;
>
> (b) a DNA encoding (a), wherein the DNA is identical in length to (a); and
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> (c) a complement of (a) or (b), wherein the complement is identical in length to the nucleic acid of (a) or (b).
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> 36. A vector **comprising** a **heterologous** sequence, wherein the **heterologous** sequence is selected from the group **consisting** of
>
> (a) SEQ ID NO: 117937;
>
> (b) a DNA encoding the nucleic acid of (a), wherein the DNA is identical in length to (a);
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> (c) a sequence at least 80% identical to (a) or (b), wherein the nucleic acid is 19-24 nucleotides in length; and
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> (d) the complement of (a)-(c), wherein the complement is identical in length to the nucleic acid of (a)-(c).

The specification of the instant application identifies SEQ ID NO: 117937 as a miRNA of 22 nucleotides identified from human herpesvirus 5 or more commonly known as human cytomegalovirus (HCMV). The specification further identifies the miRNA as being derived from

the 67 nucleotide precursor of SEQ ID NO: 4204050. The specification describes the identification of the miRNA and precursor using bioinformatic methods that have since become accepted and standard by those skilled in the art.

The Examiner characterizes Ghazal as disclosing a yeast artificial chromosome vector comprising a HCMV insert that is 229,354 nucleotides in length. The Examiner identifies nucleotides 163187-163253 of the Ghazal insert as being identical to SEQ ID NO: 4204050 and as also comprising SEQ ID NO: 117937. The HCMV insert disclosed by Ghazal is more than 3,400 times greater in size than the inserts of SEQ ID NO: 4204050 and SEQ ID NO: 117937 recited in claims 31 and 36, respectively. Applicant respectfully submits that claims 31 and 36 do not encompass Ghazal because of the drastic differences in the vector inserts.

The Examiner relies on *In re Crish*, 73 USPQ2d 1364 (Fed. Cir. 2004) to support the anticipation rejection. The Examiner characterizes *In re Crish* as the court finding that claims drawn to a purified oligonucleotide comprising a portion of SEQ ID NO: l, wherein said portion consists of the nucleotide sequence from 521 to 2473 of SEQ ID NO: 1, were anticipated by the prior art disclosure of a nucleotide sequence comprising SEQ ID NO:1 on the grounds that a "reasonable interpretation of the claims containing both of the terms "comprising" and "consists" is that the term "consists" limits the "said portion" language to the subsequently recited numbered nucleotides, but the earlier term "comprising" means that the claim can include that portion plus other nucleotides. The Examiner alleges that claims 31 and 36 have essentially the same construction as those of *In re Crish*, being drawn to a nucleic acid (vector) comprising a heterologous sequence, wherein the heterologous sequence consists of a specified SEQ ID. As a result, the Examiner concludes that Ghazal anticipates claims 31 and 36 because the instant claims "do not preclude the presence in the vector of HCMV sequences other than SEQ ID NOS: 4204050 or 117937." The Applicant respectfully disagrees. The Application respectfully submits that the Examiner has failed to consider the term "heterologous" that is present in both claims 31 and 36.

The Applicant agrees with the Examiner to the extent that the earlier open-ended transition term "comprising" allows for the claimed vector to include nucleotide sequences other than the HCMV inserts of than SEQ ID NOS: 4204050 and 117937. However, the Applicant respectfully submits that the term "heterologous" in combination with "consisting of" in claims 31 and 36 specifically precludes the addition of any other nucleotide sequence from HCMV.

Vectors are well known as vehicles for genetic material of interest. Vectors consist of an insert (i.e., the genetic material of interest) and a larger sequence that serves as the "backbone" of

the vector. The backbone of the vector often includes features such as an origin or replication, multicloning site and selectable marker. As such, an "insert" is distinct from the "backbone" of a vector. In other words, an insert is "heterologous" to the backbone of the vector.

Claims 31 and 36 specifically recite that the "heterologous sequence" of the claimed vectors **consists** of limited nucleic acids related to SEQ ID NOS: 4204050 or 117937. In other words, the insert of claims 31 and 36 is specifically limited to nucleic acids related to SEQ ID NOS: 4204050 or 117937. The backbone of the vector may certainly contain additional nucleotides, as contemplated by the earlier open-ended transition term "comprising." However, the vector may not comprise any further insert nucleotides due to the use of "consisting of" in combination with "heterologous sequence." By contrast, the claims of *In re Crish* recited that the vector comprised a "portion" of an HCMV sequence without any terms, such as "heterologous," to distinguish the insert from the backbone of the vector. As a result, the insert of claims 31 and 36 is explicitly limited to specific nucleotides whereas the insert of *Crish* could include additional nucleotides. The Applicant respectfully submits, therefore, that one of ordinary skill in the art would interpret the insert of claims 31 and 36 to be limited to SEQ ID NOS: 4204050 and 117937 with all other sequence of the vector being related to the backbone of the vector. Such a claim scope is in conformance with the specification of the instant application which contemplates the addition or insertion of a specific sequence, such as SEQ ID NOS: 4204050 and 117937, to a vector. The Ghazal vector is thus distinct from the claimed vectors. In view of the foregoing remarks, Applicant respectfully submits that the rejection of claims 31 and 36 under 35 U.S.C. §102(b) as being anticipated by Ghazal should be withdrawn.

b. 35 U.S.C. § 103

At pages 4-10 of the Office Action, the Examiner maintains the rejection of claims 26 and 33 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ghazal in view of Hogan (US 5,541,308; "Hogan") and claims 35 and 37 over Ghazal in view of Buck et al., Biotechniques 27:528-536 (1999; "Buck"). Specifically, the Examiner asserts that absent secondary considerations the claimed sequences are obvious over the more than 8,255,610 possible probes that could be created based upon the teachings of Ghazal in view of Hogan or the 1,834,676 possible probes that could be created based upon the teachings of Ghazal in view of Buck. As evidence of secondary considerations, the Applicant has previously relied on the specification reciting that SEQ ID NO: 117937 is an HCMV miRNA and that SEQ ID NO: 4204050 is a precursor therefore. In response, the Examiner asserts that there is no evidence that the claimed sequences have miRNA or

gene regulatory activity. Applicant respectfully disagrees. Applicant respectfully submits that the Examiner has impermissibly applied a higher evidentiary standard for proving nonobviousness.

The evidentiary standard for obviousness is articulated in MPEP 2142, which states the following (emphasis added):

> **If the examiner determines there is factual support for rejecting the claimed invention under 35 U.S.C. 103, the examiner must then consider any evidence supporting the patentability of the claimed invention, such as any evidence in the specification** or any other evidence submitted by the applicant. **The ultimate determination of patentability is based on the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence**. *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). The legal standard of "a preponderance of evidence" requires the evidence to be more convincing than the evidence which is offered in opposition to it. With regard to rejections under 35 U.S.C. 103, the examiner must provide evidence which as a whole shows that the legal determination sought to be proved (i.e., the reference teachings establish a prima facie case of obviousness) is more probable than not.
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> **When an applicant submits evidence, whether in the specification as originally filed or in reply to a rejection, the examiner must reconsider the patentability of the claimed invention.** The decision on patentability must be made based upon consideration of all the evidence, including the evidence submitted by the examiner and the evidence submitted by the applicant. A decision to make or maintain a rejection in the face of all the evidence must show that it was based on the totality of the evidence. Facts established by rebuttal evidence must be evaluated along with the facts on which the conclusion of obviousness was reached, not against the conclusion itself. In re Eli Lilly & Co., 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990).

As discussed above, the Examiner must consider the evidence of nonobviousness that is presented in the specification. Specifically, the Examiner must consider the teachings in the specification regarding the predicted activity of SEQ ID NOS: 4204050 and 117937. Furthermore, the Examiner must consider that at the time of filing of the instant application, miRNA prediction models had a success rate of at least 69-78% for identifying miRNA nucleic acids that are capable of binding and inhibiting expression of a target mRNA transcript, as shown by John et al., PloS Biology 2:1862-1879 (2004). Therefore, Applicant respectfully submits that the specification, by itself, provides the

necessary secondary evidence to show that nucleic acids and vectors related to SEQ ID NOS: 4204050 and 117937 are nonobviousness. In order for the Examiner to reach a finding of obviousness would erroneously require experimental certainty or 100% assurance that the claimed nucleic acids act or form a miRNA. In view of the foregoing, Applicant respectfully submits that the claimed nucleic acids related to miRNAs, precursors thereto and vectors thereof are not obvious over Ghazal in view of Hogan or Buck. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 26, 33, 35, and 37 under 35 U.S.C. §103(a).

3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

POLSINELLI SHUGHART PC

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By: /Teddy C. Scott, Jr., Ph.D./
Teddy C. Scott, Jr., Ph.D.
Registration No. 53,573
Customer No. 37808

POLSINELLI SHUGHART PC
180 N. Stetson Ave., Suite 4525
Chicago, IL 60601
312.819.1900 (main)
312.873.2913 (E-fax)
312.873.3613 (direct)